by TANVEER PADDER, MD; KENNETH SKODNEK, MD; SEEMA HASHMI, MD; MAJID SAMAD, MD; APARNA UDYAWAR, MD; NOUMAN AZHAR, MD; and KAMIL JAGHAB, MD

All from the Department of Psychiatry, Nassau University Medical Center, East Meadow, New York

Acute Akathisia with Suicidal Ideation Associated with Low Dose Aripiprazole

ABSTRACT

Akathisia is a relatively common and disturbing side effect of neuroleptic agents. It is widely assumed that the atypical antipsychotic agents are much less likely to produce movement disorders than the conventional antipsychotic agents. Still, there have been reports of akathisia associated with all of the atypical antipsychotic agents.

Like other atypical antipsychotics, aripiprazole has a low risk of producing extrapyramidal symptoms compared with the conventional antipsychotics. Aripriprazole is generally well tolerated relative to other antipsychotic medications and has low propensity to cause clinically significant side effects, including weight gain, hyperprolactinemia, and QT interval prolongation. We are reporting a case of acute akathisia along with suicidal ideations associated with a low dose of aripiprazole in a 23-year-old patient with a mood disorder. In this patient, suicidal ideations appeared suddenly for the first time concurrently with akathisia and disappeared when akathisia was treated and aripiprazole discontinued. To the best of our knowledge, this is the first reported case of akathisia with suicidal ideations associated with novel antipsychotic agent aripiprazole in the US.

ADDRESS CORRESPONDENCE TO:
Tanveer A. Padder MD, Department of Psychiatry, Nassau University Medical Center, 2201 Hempstead Turnpike, East Meadow NY 11554
Phone: (516) 572-3077; Fax: (516) 527-4725; E-mail: tanveerpadder@gmail.com

Key Words: Akathisia, aripiprazole

INTRODUCTION

Akathisia is derived from the Greek word a + kathisis, which means "not to sit."[1] It was first described by the Czech neuropsychiatrist Ladislav Haskovec in 1901 to refer to restless patients with hysteria and neurasthenia. It is a condition characterized by subjective feelings of restlessness and objective signs of restlessness.[2] It is often associated with treatment with conventional antipsychotic agents. Symptoms include feelings of anxiety, inability to relax, pacing, rocking movements, and jitteriness.[2] The patient may rock from foot to foot while standing and make shuffling movements or stamp his or her legs and feet while seated. The patient may also complain of being able to feel his or her muscles quiver.[3] The increased motor activity represents the patient's attempt to relieve feelings of inner restlessness.[1–4] Akathisia appears rapidly, and onset tends to coincide with the maximum drug concentration in the blood.[5] Although symptoms are most commonly seen in the extremities, there are reports of akathisia occurring in the abdomen[6] and in the respiratory muscles.[7] As many as 90 percent of younger patients taking typical antipsychotics develop akathisia at some time during treatment.[5] The incidence of akathisia associated with antipsychotics decreases with age; it occurs in only 15 percent of patients over age 65 years.[5] Akathisia occurred in 11 percent of patients receiving aripiprizole for acute mania and led to discontinuation in 1.6 percent of patients.[8] Five types of akathisia have been described: Acute, chronic, tardive, withdrawn, and pseudo-akathisia. The rating scales used for akathisia include the Abnormal Involuntary Movement Scale, Barnes Akathisia Scale, and the Simpson and Angus Scale for EPS.

CASE REPORT

Mr. A is a 23-year-old Hispanic man with no prior psychiatric admissions and a history of impulsive behavior who was referred to the ambulatory mental health clinic by his primary care physician for a psychiatric evaluation. The presenting complaints were irritability, impulsivity, and low frustration tolerance. Mr. A was starting a new job soon and wanted "help" to hold this job. Mr. A had a history of inability to hold a job in the past and had changed many jobs because of getting angry and his tendency to get confrontational. Mr. A claimed that he would easily get into fights and was easily provoked. He also had a history of getting into physical altercations with others over minor things. In addition to getting angry, Mr. A also reported being impulsive, getting distracted easily, being hyper, having racing thoughts, and spending money excessively in the past. Mr. A denied any neurovegetative symptoms of depression and strongly denied any suicidal/homicidal ideation. In the past, Mr. A had symptoms consistent with bipolar mixed spectrum, including depression, irritability, restlessness, impulsivity, spending sprees, and getting into fights easily but was never diagnosed with bipolar disorder. He did not give any history of acute mania or psychosis in the past. Mr. A strongly denied having any suicidal ideations, intent, or plan in the past. Mr. A admitted to having problems with attention, concentration, and making careless mistakes, although he was never diagnosed with attention deficit/hyperactivity disorder (ADHD). Mr. A's current symptoms were related to his difficulty in controlling anger and inability to focus, especially at work. There was no evidence of acute mania or psychosis during the initial interview. Mr. A denied having any medical problems except for acne and was not taking any medications. He admitted to taking paroxetine (Paxil®) and sertraline (Zoloft®), which was prescribed by his primary care physician for depression for about a month two years previously without any improvement in his mood. He did not like the medications, he said, because he felt no difference in his mood while taking them, although he denied any side effects on either drug, including akathisia. He admitted using marijuana, PCP, and alcohol in the past but strongly denied any current use. His urine toxicology

As many as 90 percent of younger patients taking typical antipsychotics develop akathisia at some time during treatment.

was negative on admission to the clinic. According to him, he only used those substances when going to "rave parties" with friends but discontinued their use because he wanted to get a job and get on with his life. Mr. A was never admitted to any psychiatric unit.

Initial mental status examination. Mr. A was a 23-year-old overweight Hispanic man who appeared his stated age and was casually dressed with facial acne. His attitude seemed somewhat hostile in the beginning; however, as the interview progressed he became quiet, friendly, and cooperative. His mood was anxious, and his affect was appropriate to setting and content. He denied perceptual disturbances and denied any auditory or visual hallucinations. His speech was normally productive, goal-directed, and relevant. He exhibited a capacity for abstract thought and appeared to be intelligent and well informed. However, he had clear difficulty in concentration and attention and struggled with the serial seven subtractions. Mr. A was well oriented to time, place, and person. His memory seemed to be intact. He denied any suicidal or homicidal ideations, intent, or plan. His impulse control was appropriate during this interview. His insight and judgment seemed to be good. He appeared to be reliable.

Mr. A's DSM-IV diagnosis was as follows: Axis I—Mood Disorder Not Otherwise Specified, Rule out Bipolar Disorder, II Mixed Type, Rule out ADHD; Axis II Cluster B Traits; Axis III Acne; Axis IV Occupational Problems; Axis V 61–70.

Mr. A was willing to take medications but was very concerned about the side effects of psychotropics, especially the weight gain and acne. He was started on aripiprazole (Abilify®) 5mg daily because of this medication's low side effect profile. He reported adherence to the medication and was tolerating it well without any acute side effects. Mr. A seemed to be doing well and reported some improvement in mood symptoms after two weeks. At that time, the option of increasing aripiprazole to 10mg daily was discussed with Mr. A. as 5mg is not the recommended dose. He reported feeling "fine" on the current dose of aripiprazole, was reluctant to take the recommended higher dose, and wanted some time to think it over. Mr. A admitted that the medication was helping him stay calm and less angry, and his mood and anxiety symptoms had also improved, although he still had problems with attention, concentration, and organization. Eventually, Mr. A agreed to take 10mg of aripiprazole daily. After taking 10mg of aripiprazole for three days, Mr. A called the clinic in great distress and reported he felt extremely restless and irritable with an inability to sit still and a constant desire to move. Mr. A also reported that he was experiencing suicidal ideations although he did not specify any plan that time. According to Mr. A, these symptoms, which he never experienced before, started suddenly. Mr. A reported that he was feeling so distressed with these symptoms he could not sit still and was moving around constantly. The suicidal ideation started a few hours after the onset of akathisia. He did not get any relief of suicidal ideation by constant moving. He felt so unsafe that he insisted his mother call 911. Mr. A was then advised to go to the nearest emergency room, and he was admitted to the psychiatric unit for stabilization. During his hospitalization, aripiprazole was discontinued and Mr. A was treated with propanolol and benzodiazepines, to which he responded very well. Once akathisia was treated and aripriprazole was discontinued, the suicidal thoughts went away as abruptly as they had appeared. Mr. A was discharged after one week and was prescribed bupropion (Wellbutrin®) and gabapentin (Neurontin®). Two months after discharge, Mr. A continued to do well on the current regimen without any akathisia-like symptoms or suicidal ideations.

DISCUSSION

Aripiprazole, a quinolinone derivative, has a unique pharmacological profile as it is a partial agonist of the D2 dopamine and 5HT1A receptors and an antagonist for the 5HT2 serotonin receptor. Aripiprazole received FDA approval in November, 2002, for the treatment of schizophrenia and the maintenance treatment of bipolar disorder with manic and mixed episodes. Akathisia can occur during treatment with many

The suicidal ideation [in our patient] started a few hours after the onset of the symptoms of akathisia.

Akathisia can occur during treatment with many different types of medications. Antipsychotics, antidepressants, and sympathomimetics have all been implicated in the development of akathisia.

different types of medications. Antipsychotics, antidepressants, and sympathomimetics have all been implicated in the development of akathisia.[2] However, the conventional antipsychotics are traditionally seen as the primary cause.[2] The estimated incidence of akathisia in patients taking conventional antipsychotics varies widely, ranging from 20 to 75 percent.[9] However, the most common estimate of incidence is around 20 percent.[10] Antipsychotic-induced akathisia is now believed to be due to an inhibition of dopaminergic neurons that are located in the ventral tegmental area but have significant input from the noradrenergic and serotonergic systems.[11] Any medication that can decrease the release of dopamine and lead to a syndrome of dopamine deficiency in the ventral tegmental area can be expected to have akathisia as a side effect.[11] Akathisia has also been reported with a number of medications that are more commonly used in other fields of medicine. Cases have been reported after the administration of antiemetic or prokinetic medications with D2 antagonist activity.[12] These agents include SSRIs, promethazine, prochlorperazine, metoclopramide, and trimethobenzamide droperidol. Other medications that have been reported to induce akathisia include steroids, some bronchodilators, and interferon.[13]

A case in which akathisia may have contributed to a patient's suicide has been reported with fluphenazine treatment[14] and a link between akathisia and suicide has been proposed.[15] Scholten, et al.,[16] has reported suicidal ideations and suicidal attempt in five patients after starting aripriprazole. These patients had not previously had suicidal attempts or ideation and suicidal thoughts disappeared after discontinuing aripiprazole. Suicidal ideations can be an inherent part of a patient's psychiatric symptoms, and it is difficult to attribute suicidal ideation to aripiprazole or akathisia based on such a small sample. It is not clear whether suicidal ideations occurred due to acute akathisia or whether aripiprazole contributed to suicidal ideations in any other way apart from causing akathisia. Further studies are needed to prove an association of akathisia and suicidal ideations in patients treated with this novel antipsychotic agent aripiprazole.

REFERENCES

1. Friedman JH, Wagner RL. Akathisia: The syndrome of motor restlessness. *Am Fam Physician* 1987;35:145–9.
2. Baldassano CF, Truman CJ, Nierenberg A, et al. Akathisia: A review and case report following paroxetine treatment. *Compr Psychiatry* 1996;37:122–4.
3. Biological therapies. In: Sadock BJ, Sadock VA (eds). *Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry, Ninth Edition.* Philadelphia, PA: Lippincott Williams & Wilkins, 2003:974–1150.
4. Barnes TR, McPhillips MA. Novel antipsychotics, extrapyramidal side effects, and tardive dyskinesia. *Int Clin Psychopharmacol* 1998;13(suppl3):49–57.
5. Jauss M, Schroder J, Pantel J, et al. Severe akathisia during olanzapine treatment of acute schizophrenia. *Pharmacopsychiatry* 1998;31:146–148[Medline].
6. Wirshing WC. Movement disorders associated with neuroleptic treatment. *J Clin Psychiatry* 2001;62(suppl21):15–18.
7. Ratey JJ, Salzman C. Recognizing and managing akathisia. *Hosp Community Psychiatry* 1984;35:975–7.
8. Keck P, March R, Kodimitris T, et al. A placebo-controlled, double-blind study of the efficacy and safety of aripriprazole in patients with acute bipolar mania. *Am J of Psychiatry* 2003;160(9):1651–8.
9. Hirose S. Restlessness of respiration as a manifestation of akathisia: Five case reports of respiratory akathisia. *J Clin Psychiatry* 2000;61:737–41.
10. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.* Washington, DC: American Psychiatric Press, Inc., 2000.
11. Brown TM, Stoudemire A, Fogel BS, Moran MG. Psychopharmacology in the medical patient. Stoudemire A, Fogel BS, Greenberg DB (eds). *Psychiatric Care of the Medical Patient, Second Edition.* New York, NY: Oxford University Press, 2000:330–72.
12. Lipinski JF Jr, Mallya G, Zimmerman P, Pope HG Jr. Fluoxetine-induced akathisia: Clinical and theoretical implications. *J Clin Psychiatry* 1989;50:339–42.
13. Anfinson TJ. Akathisia, panic, agoraphobia, and major depression following brief exposure to metoclopramide. *Psychopharmacol Bull* 2002;36:82–93.
14. Fawzy FI, Servis ME, Greenberg DB. Oncology and psychooncology. Wise MG, Rundell JR (eds). *The American Psychiatric Publishing Textbook of Consultation-Liaison Psychiatry, Second Edition.* Washington, DC: American Psychiatric Publishing, 2002:657–78.
15. Shear MK, Frances A, Weiden P. Suicide associated with akathisia and depot fluphenazine treatment. *J Clin Psychopharmacol* 1983;3:235–6.
16. Scholten MR, Selten JP. Suicidal ideations and suicidal attempts after starting with aripiprazole. *Ned Tijdschr Geneeskd* 2005;149(41):2296–8.